

**EXHIBIT A**  
**BIOGRAPHICAL SKETCH**

1/12/2006

**NAME** C.-K. James Shen

**DATE OF BIRTH** July 29, 1949

**FAMILY** Wife Chien Celia Shen  
Son Jeffrey Shen

**EDUCATION**



National Taiwan University	B.S.	1971	Chemistry
University of Calif., Berkeley	Ph.D.	1977	Biological Chemistry
California Institute of Technology	Postdoc	1978-81	Molecular Biology

**PROFESSIONAL EXPERIENCE**

1981-1983 Assistant Professor, Department of Genetics  
University of California, Davis

1981-1986 Director and Consultant, Division of Molecular Biology,  
Advanced Genetics Research Institute (AGRI), Oakland

1986-1987 Visiting Scientist, Institute of Molecular Biology  
Academia Sinica, Taipei, ROC

1983-1988 Associate Professor, Department of Genetics  
University of California, Davis

1991-1992 Visiting Professor, Department of Molecular and Cellular Physiology,  
Stanford University

1988- 1998 Professor of Genetics, Section of Molecular and Cellular Biology,  
University of California, Davis

1999- Emeritus Professor, University of California, Davis

1995- Adjunct Professor, Institute of Genetics, National Yang-Ming  
University, Taipei, ROC

1995- Adjunct Professor, Institute of Molecular Medicine, National Taiwan  
University, Taipei, ROC

2001- Scientific Advisory Board, Vita Gen Inc.

1995-2004 Director and Distinguished Research Fellow, Institute of Molecular  
Biology, Academia Sinica, Taipei, ROC

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2004- Distinguished Research Fellow, Institute of Molecular  
Biology, Academia Sinica, Taipei, ROC

#### ACADEMIC HONORS AND AWARDS

Anthony Earle C. Fellowship, 1975-1977  
NIH Postdoctoral Fellowship, 1978-1981  
NIH Research Career Development Award, 1984-1989  
NIH Fogarty Senior International Fellowship, 1986-1987  
Distinguished Research Fellow, Academia Sinica, Taipei, ROC, 1995-  
NSC Frontier of Science Research Award, Taiwan, ROC, 2000-2005  
Investigator Award, Academia Sinica, 2005-2009  
Academician, Academia Sinica, Taipei, ROC, 2000-  
Fellow, AAAS (American Association for the Advancement of Science), 2003-

#### ADMINISTRATIVE EXPERIENCE

##### US

Graduate Student Committees, total 80  
Various Faculty Search Committees, Academic Senate Committee, Academic  
Personnel Committees, Department and Section Committees  
Executive Committee, NIH Cellular and Molecular Biology Training Grant (1987-1992)  
Chancellor's Liason Committee for the Reorganization of Biological Sciences, UC  
Davis (1988-1989)

##### Taiwan

Various Academic and Administrative Committees  
Director, IMB (1994-2004)  
Coordinate Director, National Genomic Medicine Program (2004- )

#### TRAINING RECORD (1981-2004)

16 Ph.D. students  
28 Postdoctoral fellows

#### MAJOR RESEARCH ACCOMPLISHMENTS

- (1) Established the wide use of the photocrosslinking reaction of psoralen in cell biology research and biotech application.
- (2) one of the first to establish the relationship between DNA methylation and eukaryotic gene regulation.
- (3) Re-defined the mammalian  $\alpha$ -like globin gene locus domain by discovery of the  $\theta$  globin gene.
- (4) Established an active research program on mammalian globin gene regulation.
- (5) Discovered the existence of DNA methylation program in Drosophila and demonstration of its function.

#### RESEARCH INTEREST AND EXPERTISE

Eukaryotic Gene Regulation

Genomes and Chromosomes  
Mammalian Cell Differentiation and Development  
Molecular Evolution  
Molecular Cellular Neurobiology

### TEACHING

(Average 50 lectures a year, 1981-1994)

General Genetics  
Human Genetics  
Molecular Genetics  
Eukaryotic Molecular Genetics  
Various seminar courses

### PROFESSIONAL SERVICES

#### International

NIH Molecular Biology Study Section, US (1993)  
NIH Mammalian Genetics Study Section, US (1984-1985)  
Review Panel of Biology and Biotechnology, Lawrence Livermore National Laboratory,  
Livermore, California, US (1993)  
Grant Reviewing for Frontier of Sciences Program (Japan/France)  
US National Science Foundation (NSF)  
US Department of Agriculture (USDA)  
US Sea Grant Foundation  
Cancer Research UK

#### Taiwan

Coordinate Director of National Research Program on Genomic Medicine (NRPGM)  
(2001- )  
Coordinator, International Collaborative Program, NRPGM (2003- )  
Coordinator, Mol. Cell. Neurobiology Program, Academia Sinica (2005- )  
PI, The RNAi (International) Consortium  
Advisory Committee, National Core of Genomic Medicine (2004- )  
Advisory Committee, National Program on Genome and Medicine, National Science  
Council, Taiwan, ROC (1998- 2001)  
Advisory Committee, Molecular and Genome Medicine Core Laboratory, National  
Health Research Institute, Taiwan, ROC (1996- )(chair, 1996-1999)  
Advisory Committee, Institute of Molecular Biology, Academia Sinica, Taiwan, ROC  
(1997- )  
Advisory Committee, Biotechnology Program in Medicine, Academia Sinica, Taiwan,  
ROC (1995- )  
Advisory Committee, Institute of BioAgricultural Sciences, Taiwan, ROC (1998-2001)  
Advisory Committee, Institute of Zoology, Academia Sinica, Taiwan ROC (1993-1996)  
Panel, Biology Program Grants, National Science Council, Taiwan, ROC (1996- )  
Honorary Advisor, Veteran Hospital, Taipei, ROC (1995- )  
Advisory Committee, Development Fund, Executive Yuan, Taiwan, ROC (1998-2002)  
The Board of Directors, Tunghai University, Taiwan, ROC (2003- )  
Advisory Committee, Tunghai University Life Science Research Center, Taiwan,

ROC (2003- )  
Advisory Committee, Genomic Research Center, Academia Sinica, Taiwan, ROC  
(2003- )  
Advisory Committee and Steering Committee, Brain Research Center, National Yang  
Ming University, Taiwan, ROC (2003- )  
Advisory committee, Academic Affairs Committee, National Taiwan Normal  
University, Taiwan, ROC (2003- )  
Advisory Committee, Academic Affairs Committee, Ministry of Education,  
Taiwan, ROC (2003- )  
Advisory Committee, Science Education Committee, Ministry of Education,  
Taiwan, ROC (2003- )

#### EDITORIAL SERVICE

Editorial Board: Molecules and Cells (2003-), Cell Research (2004-); Analytical  
Biochemistry (1981-1987)  
Ad Hoc Manuscript Reviewers for Journals: Analytical Biochemistry/ Biochem.  
Biophys. Res. Comm/ Biochem. Biophys. Acta/ British J. of Hematology/ Cell  
Research/ Development / The Eukaryotic Cell/ Eur. J. Biochem/ Gene/  
Genome Res./ Genomics/ J. Biol. Chem/ J. Insect. Biol/ J. Mol. Evol/ Mol.  
Cells. / Mol. Cell Biol/ Mol. Repro. Dev./ Nature/ Nucleic Acids Res./ Proc.  
Natl. Acad. Sci. USA/ Science/ Trends in Genetics

#### PROFESSIONAL ASSOCIATIONS

Academician, Academia Sinica, Taipei, ROC (2000- )  
American Society of Biochemistry and Molecular Biology  
International Molecular Biology Network (IMBN) (2002~)  
Council Member, Society of Chinese Bioscientists in America (1999-2003)  
President, Society of Molecular and Cell Biology, Taiwan, ROC (1997-2001)  
President, Society of Genetics, Taiwan, ROC (1999-2000)  
President, Asian Pacific Society of Biochemistry and Molecular Biology (1999-2001)  
Society of Genetics, Taiwan, ROC  
Society of Biochemistry, Taiwan, ROC  
AAAS  
Sigma xi, US

#### INVITED SEMINARS, CONFERENCE AND SYMPOSIUM TALKS

##### 1977-2005

International	85
Taiwan	36

##### 2000-2005

##### International

Dept. of Molecular, Cell & Development Biology, UCLA, California, USA, April 26, 2001

Gordon Conference on Red Cells, New Hampshire, July 22-27, 2001

The 13<sup>th</sup> International Conference on Hemoglobin Switching, St. John's College, Oxford, September 26-30, 2002

The Korea-Japan Drosophilists' Symposium, Seoul, Korea, Oct. 17-18, 2002

Keynote, The International Symposium of Comparative Genomics, National Yang-Ming University, Taiwan, ROC, Nov. 17th, 2002

Gordon Conference on Red Cells, IL Ciocco, Italy, May 25-30, 2003

The First Symposium on Frontiers of Biomedical Science, Epigenetics in Development and Disease, Shanghai, China, October 24-26, 2003

Xiangshan Science Symposium on Genomics & Evolution, Beijing, China, October 27-31, 2003

Genome Institute, Singapore, "Transcriptome Analysis of the Mammalian Brains", May 28, 2004

10<sup>th</sup> Society of Chinese Bioscientist in American, Beijing, China, "The Eukaryotic DNMT2 Genes", July 18-23, 2004

The 14<sup>th</sup> Conference on Hemoglobin Switching, Orcas Island, Washington, "Co-Factor and Chromatin-Binding of Transcription Factors EKLF and NF-E2", Sept. 10-14, 2004

The Cell Nucleus "46<sup>th</sup> Symposium of the Society for Histochemistry", Prague, Czech Republic, "Modeling of A Transcriptionally Competent Complex in Transcriptionally Inactive Cells", Sept. 22-25, 2004

IGBMC-IMB France-Taiwan Joint Symposium, Strasbourg, France, "The Eukaryotic DNA Methylation Program-Flies to Mammals", Sept. 20-21, 2004

HUGO Pacific Meeting, Singapore, "High Troughput Analysis of Mammalian Brain-Expressed Genes", Nov. 17-20, 2004

JBS International Symposium on Transcription, "Sumoylation of the Erythroid Transcription Factor P45/ NF-E2", Kusatsu, Japan, Jan. 10-12, 2005

CDB Taiwan-Japan Bi-Lateral Symposium, "DNA Methylation Program: Flies to Mammals", Riken, Japan, Jan. 13-14, 2005

National University of Singapore, Division of Biological Sciences, "Transcriptional Regulation of Human Globin Gene Switch-EKLF and p45/ NF-E2 In Play", May 5-7, 2005

The 5<sup>th</sup> Across the Taiwan Strait Symposium on Cell Biology, "Regulation of Human Globin Switch-Transcription Factors and Gene Positioning in Play", Fujian, China, Oct. 29-30, 2005

Taiwan-France Joint Symposium on Transcription and Diseases, "Regulation of transcription by factor modification and gene positioning", Academia Sinica, Taipei, Taiwan, ROC, Nov. 17-18, 2005

#### Taiwan

錢思亮紀念演講會，基因與基因體研究廿一世紀生物學家的兒童樂園，Feb.11, 2000.

Genomic Medicine Symposium, National Yang-Ming University, Drosophila and Mammalian Protein Factors Recognizing m<sup>5</sup>CpG DNA: Functional and Structural Parallels, May 29-31, 2000.

National Taiwan Medical School, Basis and treatment of Human Genetic Desises: Globin Gene families as a paradigm, Sept. 20, 2000.

Society of Biochemistry and Molecular Biology, Taiwan, Drosophila Protein Related to Components of the Vertebrate DNA Methylation Program, Nov. 3-5, 2000.

Keynote, 16<sup>th</sup> Biomedical Science Symposium, Molecular Genetics of Human Globin Gene Switch: Implications for Therapy of Hemoglobinopathies, March 24, 2001.

Institute of Molecular, Signal Transduction in Human Globin Switch, April 6, 2001.

Dept. of Life Science, National Chung Hsing University, Taichung, Eukaryotic DNA Methylation-New Perspectives, June 1, 2001.

Tunghai University, Taichung, Development Switch of the Mammalian Globin Gene Family: A Complex Molecular and Cellular Problem, Oct. 15, 2001.

Institute of Molecular Biology, Academia Sinica, Taipei, A Novel Cassette for Erythroid Gene Expression, Dec. 14-15, 2001.

Institute of Molecular Biology, Academia Sinica, Taipei, The Mammalian DNA Methylation Program-Lessons from the Flies, Dec. 18-19, 2001.

Chung Shan Medical University, Taichung, DNA Methylation and Disease, May 17, 2002.

Taipei International Council, World Trade Center, Taipei, 二〇〇二年台北國際生物科技菁英論壇演講, June 24, 2002.

Academia Sinica, Taipei, Academician Lecture, July 5, 2002.

Department of Zoology, National Taiwan University, June 5, 2003.

National Taiwan Normal University, Taipei, 泰山文化基金會邀請演講, Oct. 29, 2003.

台中中山醫學大學演講, 人類紅血球基因調控機制之研究, April 23, 2004.

慈濟大學院週會演講, "High Throughput Analysis of Brain Expressed Genes", Dec. 10, 2004.

National Taiwan Medical College, National Taiwan University, Human Globin Gene Switch-Basic and Medical Implications, Dec. 22, 2004.

Symposium on Developmental Biology, Tunghai University, April 8-9, 2005.

#### GRANT SUPPORT

##### Past

American Cancer Society, "Molecular Genetic of Human Actin Gene Family" (1984-1986)

California Biotechnology Training Grant, "DNA Supercoiling in Mammalian cells" (1986)

NIH Research Career Development Award, US Public Health (1984-1989)

NIH, US Public Health, "Evolution and Regulation of Primate Globin Gene Families" (1981-1999)

National Science Council Grant, Taiwan, ROC "Erythroid Gene Regulation" (1995-1999)

Frontier of Science Research Award, NSC, Taiwan, ROC "DNA CpG MTases and DNA methylation in Eukaryotic Development" (2000-2005)

##### Current

National Science Council, Academia Sinica, Genomics Program, "Novel Genes in Mammalian Brain Structure and Function" (2000-2010)

National Health Research Institute, Taiwan, ROC "Human Globin Gene Switch" (1996-2005)

Investigator Award, Academia Sinica, Taiwan, ROC "Molecular and Cellular Basis of Neuro development and neuro degeneration" (2005-2009)

PUBLICATIONS

1. Shen, C.-K.J., Wieschahn, G. and Hearst, J.E.. (1976) Cleavage Patterns of Drosophila melanogaster satellite DNAs by restriction enzymes. *Nucleic Acids Res.* 3, 931-952.
2. Hanson, C.V., Shen, C.-K.J. and Hearst, J.E. (1976) In situ crosslinking of DNA as a probe for chromatin structure. *Science* 193, 62-64.
3. Shen, C.-K.J. and Hearst, J.E. (1976) Psoralen cross-linked secondary structure map of single-stranded virus DNA. *Proc. Natl. Acad. Sci. USA* 73, 2649-2653.
4. Shen, C.-K.J. and Hearst, J.E. (1977) Detection of long range sequence order in Drosophila melanogaster satellite DNA IV by photochemical reaction and denaturation microscopy. *J. Mol. Biol.* 112, 495-507.
5. Isacacs, S.T., Shen, C.-K.J. Hearst, J.E. and Rapoport, H. (1977) Synthesis and characterization of new psoralen derivatives with superior photoreactivity with DNA and RNA. *Biochem.* 16, 1058-1064.
6. Shen, C.-K.J. and J.E. Hearst. 1977. Mapping of sequences with two-fold symmetry on the simian virus 40 genome: a photochemical cross-linking approach. *Proc. Natl. Acad. Sci. USA* 74:1363-1367.
7. Shen, C.-K.J. and Hearst, J.E. (1977) Chromatin structures of mainband and satellite DNAs in Drosophila melanogaster nuclei as probed by photochemical cross-linking of DNA with troxsalen. *Cold Spring Harbor Symposium Quantitative Biology* XLII, 179-189.
8. Shen, C.-K.J., Hsieh, T.-S., Wang, J.C. and Hearst, J.E. (1977) Photochemical cross-linking of DNA-RNA helices by psoralen derivatives. *J. Mol. Biol.* 116, 661-679.
9. Shen, C.-K.J. and Hearst, J.E. (1978) Photochemical cross-linking of transcription complexes with psoralen. I. Covalent attachment of in vitro SV40 nascent RNA to its double-stranded DNA template. *Nucleic Acids. Res.* 5, 1429-1441.
10. Shen, C.-K.J., Ikoku, A.S. and Hearst, J.E. (1979) A specific DNA orientation in the filamentous bacteriophage fd as probed by psoralen cross-linking and electron microscopy. *J. Mol. Biol.* 127, 163-175.
11. Shen, C.-K.J. and Hearst, J.E. (1979) A technique for relating long range base pairing on single-stranded DNA and eukaryotic RNA processing. *Anal. Biochem.* 95, 108-116.
12. Lauer, J., Shen, C.-K.J. and Maniatis, T. (1980) Chromosomal arrangement of human  $\alpha$ -like globin genes: sequence homology and  $\alpha$ -globin gene deletion. *Cell* 20, 119-130.
13. Shen, C.-K.J. and Maniatis, T. (1980) Tissue specific DNA methylation in cluster of rabbit  $\beta$ -like globin genes. *Proc. Natl. Acad. Sci. USA.* 77, 6634-6638.
14. Shen, C.-K.J. and Maniatis, T (1980) The organization of repetitive sequences in a cluster of rabbit  $\beta$ -like globin genes. *Cell* 19, 379-391.

15. Fritsch, E.F., Shen, C.-K.J., Lawn, R.M. and Maniatis, T. (1981) The organization of repetitive sequence in mammalian globin gene clusters. *Cold Spring Harbor Symposium Quantitative Biology* 45, 762-775.
16. Shen, C.-K.J. and Maniatis, T. (1982) The organization, structure and in vitro transcription of Alu family RNA polymerase III transcription units in the human  $\alpha$ -like globin gene cluster: Precipitation of in vitro transcripts by lupus anti-la antibodies. *J. Mole. Appl. Genet.* 1, 343-360.
17. Shen, C.-K.J. and Maniatis, T. (1982) Nucleotide sequence, DNA modification and in vitro transcription of Alu family repeats in the human  $\alpha$ -like globin gene cluster. In Genetic Engineering Techniques Recent Developments, eds. R.C. Huang, T.T. Kuo, and R. Wu, Academic Press, 129-158.
18. Fox, F.M., Hess, J.F., Shen, C.-K.J. and Schmid, C.W. (1983) Alu family members in the human  $\alpha$ -like globin gene cluster. *Cold Spring Harbor Symposium of Quantitative Biology* 47, 1131-1134.
19. Hess, J.F., Fox, G.M., Schmid, C.W. and Shen, C.-K.J. (1983) Molecular evolution of the human adult  $\alpha$ -like globin gene region - insertion and deletion of the Alu family repeats and non-Alu DNA sequences. *Proc. Natl. Acad. Sci. USA* 80, 5970-5974.
20. Shen, C.-K.J. (1983) Superhelicity induces hypersensitivity of a human polypyrimidine polypurine DNA sequence in the human  $\alpha 2$ - $\alpha 1$  globin intergenic region to S1 nuclease digestion-high resolution mapping of the clustered cleavage sites. *Nucleic Acids Res.* 11, 7899-7910.
21. Sawada, I., Beal, M.P., Shen, C.-K.J., Chapman, B., Wilson, A.C. and Schmid, C. (1983) Intergenic DNA sequences flanking the pseudo  $\alpha$  globin genes of human and chimpanzee. *Nucleic Acids Res.* 11, 8087-8101.
22. Perez-Stable, C., Ayres, T.M. and Shen, C.-K.J. (1984) Distinctive sequence organization and functional programming of an Alu repeat promoter. *Proc. Natl. Acad. Sci. USA* 81, 5291-5295.
23. Hess, J.F., Schmid, C. and Shen, C.-K.J. (1984) Gradient of sequence divergence in the human adult  $\alpha$ -globin duplication units. *Science* 226, 7-10.
24. Shen, C.-K.J. (1985) DNA methylation and developmental regulation of eukaryotic globin gene transcription. In DNA methylation, eds. A. Riggs, H. Cedar and A. Razin. Springer-Verlag, pp. 249-268.
25. Schmid, C. and Shen, C.-K.J. (1985) The evolution of interspersed repetitive DNA sequences in mammals and other vertebrates. In: Molecular Evolution Genetics, ed. R.J. McIntyre. Plenum Publ. Inc. pp. 323-358.
26. Hess, J.F., Perez-Stable, C., Wu, G., Weir, B., Tinoco, I. Jr. and Shen, C.-K.J. (1985) A new type of RNA polymerase III-dependent transcriptional terminator: biochemical and evolutionary implications. *J. Mol. Biol.* 184, 7-21.

27. Hess, J.F., Perez-Stable, C., Deisseroth, A. and Shen, C.-K.J. (1985) Characterization of an unique RNA initiated upstream from the human  $\alpha$ 1-globin gene--polymerase II dependence, tissue specificity, and subcellular distribution. *Nucleic Acids Res.* 13, 6059-6074.
28. Willard, C., Wong, E., J., Hess, F. C.-K.J. Shen, Chapman, B., Wilson, A.C. and Schmid, C.W. (1985) Comparison of human and chimpanzee  $\xi$ 1 globin genes. *J. Mol. Evol.* 22, 309-315.
29. Sawada, I., Willard, C., Shen, C.-K.J., Chapman, B., Wilson, A., and Schmid, C.W. (1985) Evolution of alu family repeats since the divergence of human and chimpanzee. *J. Mol. Biol.* 22, 316-322.
30. Shen, C.-K.J. and Hu, W.-S. (1986) DNA supercoiling of recombinant plasmids in mammalian cells. *Proc. Natl. Acad. Sci. USA* 83, 1641-1645.
31. Marks, J., Shaw, J.-P. and Shen, C.-K.J. (1986) The orangutan adult  $\square$ -globin gene locus: Duplicated functional genes and a new member of the primate  $\square$ -globin gene family. *Proc. Natl. Acad. Sci. USA* 83, 1413-1417.
32. Perez-Stable, C. and Shen, C.-K.J. (1986) Competitive and cooperative functioning of the two promoter elements of a human Alu family repeat. *Mol. Cell. Biol.* 6, 2041-2052.
33. Marks, J., Shaw, J.-P. and Shen, C.-K.J. (1986) The primate alpha globin-like gene  $\theta$ 1: Novel sequence organization and genomic complexity. *Nature* 321, 785-788.
34. Marks, J., Shaw, J.-P. Perez-Stable, C., Hu, W.-S., Ayres, T.M., Shen, C.C. and Shen, C.-K.J. (1986) The primate  $\alpha$  globin family: A paradigm of genomic fluidity. *Cold Spring Harbor Symposium Quantitative Biology* 51, 499-508.
35. Hu, W.-S. and Shen, C.-K.J. (1987) Reconstruction of human  $\alpha$ -thalassemia genotypes in monkey cells. *Nucleic Acids. Res.* 15, 2989-3008.
36. Shaw, J.-P., Marks, J. and Shen, C.-K.J. (1987) Evidence that the recently discovered  $\theta$ 1 gene is functional in higher primates. *Nature* 326, 717-720.
37. Shaw, J.-P., Marks, J., Mohandas, T., Sparkes, R. and Shen, C.K.J. (1987) The adult  $\alpha$ globin gene loci from monkey to man. In *Prog. Clin. Biol. Res.*, eds. A. Nienhuis and G. Stamatoyannopoulos, Alan R. Liss, Inc., NY, 251, 65-80.
38. Gomez-Pedrozo, M., Mohandas, T., Sparkes, R., Shaw, J.-P., Hess, J.F., Ayres, T.M. and Shen, C.-K.J. (1987) Evolution of human cytoplasmic actin gene sequences: chromosomal mapping and structural characterization of three cytoplasmic actin-like pseudogenes including one on the Y chromosome. *J. Human Evolution* 16, 215-230.
39. Hsu, S.-L., Marks, J., Shaw, J.-P., Tam, M., Higgs, D.R., Shen, C.C. and Shen, C.-K.J. (1988) Structure and expression of human  $\theta$ 1 globin gene. *Nature* 331, 94-96.
40. Perez-Stable, C., Shen, C.C. and Shen, C.-K.J. (1988) Enrichment and depletion of *Hela* topoisomerase I recognition sites among specific types of DNA elements. *Nucleic Acids. Res.* 16, 7973-7993.

41. Gomez-Pedrozo, M., Hu, W.-S. and Shen, C.-K.J. (1988) Recombinational resolution in primate cells of two homologous human DNA segments with a gradient of sequence divergence. *Nucleic Acids Res.* 16, 11237-11247.
42. Shaw, J.-P., Marks, J., Shen, C.C. and Shen, C.-K.J. (1989) Anomalous and selective DNA mutations of the Old World Monkey  $\alpha$  globin genes. *Proc. Nat. Acad. Sci. USA* 86, 1312-1316.
43. Shen, C.C., Bailey, A., Kim, J.-H., Yuan, C.-Y., Marks, J., Shaw, J.-P., Klisak, I., Sparkes, R. and Shen, C.-K.J. (1989) The human  $\alpha 2$ - $\alpha 1$ - $\theta 1$  globin locus: some thoughts and recent studies of its evolution and regulation. In *Prog. Clin. Biol. Res.*, eds. A. Nienhuis and G. Stamatoyannopoulos, Alan R. Liss, Inc., NY 316B, 19-32.
44. Kim, J.-H., Yu, C.-Y., Bailey, A., Hardison, R. and Shen, C.-K.J. (1989) Unique sequence organization and erythroid cell-specific factor-binding of mammalian  $\theta 1$  globin promoter. *Nucleic Acids Res.* 17, 5687-5700.
45. Shen, C.-K.J. (1989) Molecular evolution of higher primates: The  $\alpha 2$ - $\alpha 1$ - $\theta 1$  locus. In *The Molecular Evolution*, ICN-UCLA Symposium, eds. M.T. Clegg and S.J. O'Brien, Alan R. Liss, Inc., pp. 75-83.
46. Yu, C.-Y., Chen, J., Lin, L.-I., Tam, M. and Shen, C.-K.J. (1990) Cell-type specific protein-DNA interactions in the human  $\xi$  globin upstream promoter region: Displacement of Sp1 by the erythroid specific factor of NF-E1. *Mol. Cell. Biol.* 10, 282-294.
47. Shen, C. and Shen, C.-K.J. (1990) Specificity and flexibility of the recognition of DNHelical structure by eukaryotic topoisomerase I. *J. Mol. Biol.* 212, 67-78.
48. Yu, C.-Y., Motamed, K., Chen, J., Bailey, A.D. and Shen, C.-K.J. (1991) The CACC box upstream of human embryonic  $\epsilon$  globin gene binds Sp1 and is a functional promoter element *in vitro* and *in vivo*. *J. Biol. Chem.* 266, 8907-8915.
49. Shaw, J.-P., Marks, J. and Shen, C.-K.J. (1991) The adult  $\alpha$ -globin locus of Old World monkeys: An abrupt breakdown of sequence similarity to human is defined by an insertion site of human Alu family repeat. *J. Mol. Evol.* 33, 506-513.
50. Reddy, S. and Shen, C.-K.J. (1991) Protein-DNA interactions *in vivo* of an erythroid-specific, human  $\beta$ -globin locus enhancer. *Proc. Natl. Acad. Sci. USA*. 88, 8676-8680.
51. Bailey, A.D., Stanhope, M., Slightom, J.L., Goodman, M., Shen, C.C. and Shen, C.-K.J. (1992) Tandemly duplicated  $\alpha$  globin genes of gibbon. *J. Biol. Chem.* 267, 18398-18406.
52. Chu, C. and Shen, C.-K.J. (1993) DNA methylation: Its possible functional roles in developmental regulation of human globin gene families. In *DNA Methylation: Its Biological Significance*, eds. Host, J.-P. and Salaz, H.P., Berkhauser Verlag, pp. 385-403.
53. Motamed, K., Bastiani, C., Zhang, Q., Bailey, A.P. and Shen, C.-K.J. (1993) CACC box and enhancer response of the human embryonic  $\epsilon$  globin promoter. *Gene* 123, 235-240.

54. Reddy, S. and Shen, C.-K.J. (1993) Erythroid differentiation of MEL cells results in re-organization of protein-DNA complexes in the mouse  $\beta^{\text{maj}}$  globin promoter but not its distal enhancer. *Mol. Cell Biol.* 13, 1093-1103.
55. Zhang, Q., Reddy, S., Yu, C.-Y., Bastiani, C., Higgs, D., Stamatoyannopoulos, G., Papayannopoulou, T. and Shen, C.-K.J. (1993) Transcriptional activation of human  $\zeta 2$  globin promoter by the  $\alpha$  globin regulatory element (HS-40): Functional role of specific nuclear factor-DNA complexes. *Mol. Cell Biol.* 13, 2298-2308.
56. Bailey, A.D. and Shen, C.-K.J. (1993) Sequential insertion of the Alu family repeats into specific genomic sites of higher primates. *Proc. Natl. Acad. Sci. USA* 90, 7205-7209.
57. Reddy, S., Stamatoyannopoulos, G., Papayannopoulou, T., and Shen, C.-K.J. (1994) Genomic footprinting and sequencing of human  $\beta$ -like globin gene locus: Tissue specificity and cell like artifact. *J. Biol. Chem.* 269, 8287-8295.
58. Zhang, Q., Rombel, I., Reddy, G. N., Gang, J.-B. and Shen, C.-K.J. (1995) Functional roles of in vivo footprinted DNA motifs within an  $\alpha$ -globin enhancer. *J. Biol. Chem.* 270, 8501-8505.
59. Rombel, I., Hu, K.-Y., Zhang, Q., Papayannopoulou, T., Stamatoyannopoulos, G. and Shen, C.-K.J. (1995) Transcriptional activation of human adult  $\alpha$ -globin genes by hypersensitivity site-40 enhancer: Function of nuclear factor-binding motifs occupied in erythroid cells. *Proc. Natl. Acad. Sci. USA* 92, 6454-6458.
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